THE CHEMISTRY OF THE NUCLEIC ACIDS AND NUCLEOPROTEINS

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This contribution makes no attempt to be a complete compendium of the literature but is designed as a critical survey of the present position in a few main sections of this field. Considerable difficulties and delays have been encountered in obtaining copies of certain journals and any omissions on this score are regretted.

NUCLEOPROTEINS AND NUCLEIC ACIDS

Isolation of nucleoproteins.—Many methods for isolating nucleoproteins involve a stage, either during the extraction or more generally in the precipitation process, which is relatively drastic and may produce an alteration in the chemical and physical properties of the nucleoprotein; thus the majority of preparations involve precipitation of the extracted material with hydrochloric or acetic acids. The extraction processes vary considerably and employ water (1 to 13), dilute alkaline solution (14 to 17), sodium chloride solution (18, 19, 20), or buffer solutions of pH values ranging from 4 to 11 (21 to 26), followed in each case by precipitation with acid. It has been suggested (27) that nucleoproteins prepared thus are of variable composition, the precipitated nucleic acid carrying with it varying quantities of loosely bound protein, and these methods are now considered unsatisfactory (28) in view of the possible rupture of the nucleic acid-protein bond during the acid precipitation. A more controlled extraction of liver nucleoprotein is that in which the tissue was treated with a solution containing 0.03*M* sodium bicarbonate and 0.5*M* potassium chloride (29, 30) and the nucleoprotein precipitated by adjusting the solution to pH 4.2. Even these conditions may, however, be too drastic, and more recently attention has been concentrated on modifications of the original mild methods (1 to 11, 15), coupled with precipitation of the nucleoprotein with saturated ammonium sulphate (12, 31) or calcium chloride (6, 7, 32) solutions. Thus an early method (32) has been modified (33) whereby fresh pulped calf thymus is extracted with water at 5° C. for twenty-four to thirty-six hours, and after clarification of the extract the nucleoprotein is pre-

differentiation of the cell, and from which, for instance, the secretory granules of the pancreas are derived.

An interesting aspect of the nucleic acids of bacterial cells has been revived recently. For some time it has been known that Gram-positive pneumococci can become Gram-negative, and this change was brought about by extracting the cells in neutral solution (20) and by an enzyme, apparently identical with the pancreas enzyme which acts upon yeast ribonucleic acid (226). The material released into the solution during the former process contained pentose nucleic acid and a nucleoprotein (20, 227). A similar change has now been effected in yeast cells and Gram-positive bacteria by extraction with a solution of a bile salt (228), and it was also possible to restore the Gram-positive reaction by replacing the responsible material, an essential component of which appears to be the magnesium salt of a pentose nucleic acid; other salts of nucleic acid could not be plated back in this way. In agreement with the previous workers, the stainable material could be progressively extracted, that part on the surface of the cell being removed first.

Induced Transformation of Pneumococcal Types

Among micro-organisms, the most striking example of the reproducible and controllable induction of inheritable and specific alterations in cell structure and function is the transformation of specific types of pneumococcus. This type of change has been brought about both *in vivo* and *in vitro*, and analogous transformations have been carried out in the field of viruses (for references, see 62). Avery, MacLeod & McCarty (62) have now isolated from type III pneumococci a biologically active fraction which in exceedingly minute amounts is capable under appropriate conditions of inducing the transformation of unencapsulated R variants of pneumococcus type II into fully encapsulated S cells of type III. Other variants are not transformed in this way. Examination of the active extract indicated, within the limits of the methods employed, that protein, unbound lipoid, and serologically active polysaccharide were absent, and that it consisted principally, if not solely, of a sodium salt, in homogeneous viscous form, of a desoxypentose nucleic acid of molecular weight of the order of 500,000. It is possible, as the authors suggest, that the biological activity of the material is not an inherent property of the nucleic acid but is due to minute amounts of some other substance so intimately associated with it as to escape detection. If, however, as

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the evidence strongly suggests, the transforming principle is a sodium salt of a desoxypentose nucleic acid, this type of polynucleotide must be regarded not merely as structurally important but as functionally active in determining the biochemical activities and specific characteristics of pneumococcal cells. This would appear to be the first occasion on which specific transformation has been experimentally induced *in vitro* by a chemically defined substance, and its implications are of the greatest importance in the fields of genetics, virology, and cancer research.

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